THE TREATMENT OF TETANUS BY MAGNESIUM SULPHATE.

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THE treatment of tetanus by magnesium sulphate was suggested by the discovery, by Dr. S. J. Meltzer, of the marked action of this salt, when applied to nerve-tissues, in inhibiting both afferent and efferent impulses.

Although similar effects can be produced by subcutaneous or intravenous injections, they are accompanied by symptoms due to the depressing effect of the drug upon the higher centers, both in the medulla and cerebrum. The action on the medulla produces slowing of respiration and finally death by paralysis of the respiratory center.

In lumbar injections into the subdural space, the drug acts directly upon the nerve-trunks at the site of injection, as is evidenced by paralysis of motion and sensation in the lower extremities, and as it diffuses itself upward along the cord, the paralysis extends to the trunk and upper extremities, diminishing, however, in intensity as it progresses.

Absorption of magnesium sulphate from the spinal canal is fairly slow, and definite action upon the nerve-trunks may be obtained while the general effects upon the higher centers may not manifest themselves for several hours or may be wholly absent. In fact, Meltzer has found that the magnesium sulphate may be removed from the spinal canal by puncture and washing, after the desired local effects have been obtained, and the undesirable action upon the higher centers wholly prevented or stopped, if already commenced. On the other hand it has been demonstrated by Dr. Teague, in experiments carried out in the Surgical Research Laboratory of Columbia University, that the drug is, to a certain extent, cumulative in its action.

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For instance, a dose insufficient in itself to produce symptoms when injected into the peritoneal cavity of guinea-pigs, will produce death when repeated at the end of twenty-four hours. In the treatment of tetanus, the dose is ordinarily repeated and this fact should be borne in mind.

Meltzer found that one cubic centimeter of a 25 per cent. solution of magnesium sulphate to every twenty-five pounds bodyweight was sufficient, when injected into the spinal canal, to produce in most cases anæsthesia to the surgical degree from the neck down. As reported in a former paper,[1] I have found a marked variation in the effects of the drug,—for instance, a similar amount per pound of bodyweight produced no anæsthesia and very slight motor-paralysis in one patient, while in another its action was most profound, producing unconsciousness which lasted nineteen hours and paralysis of motion and sensation persisting for over forty-five hours. Age and sex seem to have a direct bearing upon its action and in the same paper I made the following statement: "As far as can be learned from our present experience, children are quite susceptible, and women more so than men. The dose for a child should probably never exceed one cubic centimeter for every twenty-five pounds bodyweight, the dose for a woman should not be less, while the dose for a male adult should probably not be less than a cubic centimeter for every twenty pounds." In the treatment of tetanus, the dose usually has to be repeated and consequently may be corrected, so the uncertainty in regard to its effect is not so important as it otherwise might be. While uncertainty as to its effects might contraindicate its use for the less dangerous conditions, tetanus is attended by such a great mortality that we are justified in using anything that promises to be beneficial.

It is unfortunate that we are unable to derive much information from experimental work with animals, since the anatomical peculiarities preclude intraspinal injections except in monkeys. Dr. Teague has found that intraperitoneal injections in guinea-pigs produce little or no effect on the convulsions in induced tetanus unless a lethal dose is given. For instance, if a local tetanic spasm of a limb is induced by the injection of tetanus toxine, it cannot be controlled by an intraperitoneal injection of magnesium sulphate unless in excessive doses.

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[1] Jour. Surg., Gyn. and Obstetrics, May, 1906.

From our experience in human tetanus, we know that intraspinal injections relieve spasm, so that we must infer that it produces a block of nerve-impulses by direct action on the nerve-trunks. So far, its employment in human tetanus has not been attended by uniform results. This fact may be due to different degrees of susceptibility on the part of the patient and partly by variations in technique or lack of experience in the use of magnesium sulphate on the part of the medical attendant. As far as I can ascertain, only four cases of tetanus have been treated with magnesium sulphate. The first was treated by myself at the Roosevelt Hospital and this together with a case treated by Dr. F. H. Markoe at the New York Hospital, are reported in full by me in the *Journal of Surgery, Gynecology, and Obstetrics* for May, 1906. Since then, the report of two other cases by Dr. Samuel Logan, of New Orleans, has appeared in the *Journal of the American Medical Association* for May 19, 1906. In addition to these four cases of tetanus, a case of miliary tuberculosis, with symptoms closely resembling those of tetanus, has been treated by me and is interesting in demonstrating the effect of the drug upon the convulsions. Of these patients, only one has recovered, namely, the first patient treated by myself.

A detailed report of these cases in the present paper would require too much time, and I consequently limit myself to a statement of my deductions derived from the study of them. In my patient, a case of acute tetanus in a boy fifteen years of age, starting in a wound of the hand, we were either very fortunate in hitting upon the correct dose or else the patient was peculiarly susceptible to the action of the drug. There is not the slightest doubt in my own mind, or in the minds of those who observed the patient, that the drug had a very marked effect in inhibiting the convulsive seizures, relieving pain and producing rest. For instance, the patient at the beginning of the treatment was in a condition of practically constant opisthotonos, with rigid scaphoid abdomen and well-marked trismus. Rest and nutrition were impossible. The effect of magnesium sulphate was to produce complete relaxation of the muscles of the trunk and the extremities and considerable relaxation of the muscles of the jaw, so much so that the patient rested quietly and could swallow easily.

The injections controlled the convulsions in this patient for periods varying from twenty-nine to thirty-seven hours each. At the latter part of these periods the convulsions would begin to return and gradually increase in severity until they reached a point when it was deemed wise to give another injection. No injurious effects were noted in this patient except that throughout the treatment there was, as might be expected, paralysis of the bladder. The dose was the same as recommended by Dr. Meltzer for the production of anæsthesia. At the time the injections of magnesium sulphate were stopped, the patient was running along with the symptoms we would expect in an ordinary case of chronic tetanus. At one time, six days after the last injection of magnesium sulphate, the convulsions became more severe and magnesium sulphate was given again with similar effect. Before commencing treatment with magnesium sulphate in this patient, he was given several injections of tetanus antitoxine, one of them into the cervical cord with no apparent effect.

My impressions from observing this patient were that with the aid of magnesium sulphate we were able to keep up nourishment and strength, so that his vital forces could control the disease, and that in reaching this control the injected antitoxine was probably a great aid. According to Norris, death in tetanus may occur in a convulsion and be due to asphyxia or spasm of the heart, or, on the other hand, in about half the cases it is due to exhaustion. Exhaustion may be caused by excessive convulsions and by lack of nourishment. In such cases, judging by our experience in the case just reported, magnesium sulphate will be a great help. There are, however, a certain number of cases of tetanus which die in the first few days of the disease and which die in a condition of asthenia which can hardly be attributed to exhaustion from convulsions or from lack of nourishment. In these cases death seems to be due to a depressing action of the toxins, and magnesium sulphate would probably be of no benefit. Dr. Markoe's case is an example of this class. In this case a moderate dose of magnesium sulphate was given fifteen hours after the initial symptoms of the disease, with only a slight effect upon the convulsions, the patient dying thirteen hours later, the entire illness lasting twenty-eight hours. There were no symptoms referable to an overdose of magnesium sulphate.

In Case I, reported by Dr. Logan, death occurred at the end of the fourth day of the disease with symptoms of heart failure and hyperpyrexia. Two injections of magnesium sulphate were given. The first, about forty-one hours before death, produced complete relaxation even of the jaws, and relieved the pain completely for over twelve hours. The tonic spasm then returned rapidly in the trunk and extremities. Eighteen hours after the injection the general spasm was marked and there was twitching on attempting to swallow. The second injection was given twenty-four hours after the first and again produced complete relaxation, which lasted until his death, sixteen hours later, with the exception of a general convulsion induced by giving an enema two hours after the last injection of magnesium sulphate.

This patient's condition although somewhat improved by the first injection, grew progressively worse after the second. There was excessive bronchorrhea, the respirations were rapid and shallow, the heart's action feeble. The respiration was not slowed as is usually the case with large doses of magnesium sulphate.

An analysis of the treatment in this case is noteworthy. The patient was a boy eleven years of age; the bodyweight was estimated at eighty pounds. On the first day of the disease he was given fifty cubic centimeters of antitetanic serum by lumbar puncture. In the thirty-six hours preceding the injection of magnesium sulphate he had received 170 grains of chloral and 450 grains of bromide without effect upon the convulsions. Both injections of magnesium sulphate were given under general anæsthesia. Fifty cubic centimeters of antitetanic serum were given at the same time with the first injection. The duration of the first anæsthesia was forty minutes, of the second, thirty-five. Possibly the large doses of chloral may have depressed the heart's action and that together with the ether may have caused the bronchorrhea. It is not necessary to give an anæsthetic to perform lumbar puncture, and one of the advantages of magnesium sulphate is that it produces sufficient anæsthesia for redressment of the wound. The dose of magnesium sulphate was large, one cubic centimeter of the 25 per cent. solution for every twenty pounds at the first dose, and one cubic centimeter for every twenty-four pounds bodyweight at the second dose. Possibly its action may have been cumulative, inasmuch as the dose was repeated in twenty-four hours. The action of the second dose was, certainly, very profound.

In the second case reported by Dr. Logan there was absolutely no result from the use of magnesium sulphate. The patient was a woman, twenty-four years of age, and received a dosage corresponding to one cubic centimeter for every twenty-five pounds bodyweight. The first injection producing no result, it was followed, seventeen hours later, by another, the patient dying of failure of respiration in a tetanic seizure a short time afterward. Although this last was a severe case, there should have been some result, and the failure of the magnesium sulphate is apparently another instance of the unreliability that has been demonstrated in its use for producing anæsthesia.

In the case of general miliary tuberculosis resembling tetanus already mentioned, magnesium sulphate was quite efficient in controlling the convulsions and was repeated nine times in eight days, once with an interval of only thirteen hours, without producing untoward symptoms.

My impression of the drug is that although we cannot be certain of its effect, yet it is reasonably safe and offers us a means of modifying the convulsions and relieving pain in a way no other drug has approached. For these reasons alone it is worthy of a more extended trial. It is not a specific treatment, but it produces anæsthesia, which may be taken advantage of for intraneural or other injections of tetanus antitoxine and for revising the site of the infection.